

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION See paragraph 2 below

International application No.
PCT/EP2004/007819

International filing date (day/month/year)
09.07.2004

Priority date (day/month/year)
11.07.2003

International Patent Classification (IPC) or both national classification and IPC
C07J3/00, A61K31/56, A61P5/44, C07D239/20

Applicant

GLAXO GROUP LIMITED

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
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Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - a sequence listing
 - table(s) related to the sequence listing
 - b. format of material:
 - in written format
 - in computer readable form
 - c. time of filing/furnishing:
 - contained in the international application as filed.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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Box No. II Priority

1. The following document has not been furnished:

- copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).
 translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application,
 claims Nos. 18

because:

- the said international application, or the said claims Nos. 18 only with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (specify):
 the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 no international search report has been established for the whole application or for said claims Nos.
 the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

- the written form has not been furnished
 does not comply with the standard
the computer readable form has not been furnished
 does not comply with the standard

- the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
 See separate sheet for further details

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | |
|-------------------------------|-------------|------------|
| Novelty (N) | Yes: Claims | 1-22 |
| | No: Claims | |
| Inventive step (IS) | Yes: Claims | 1-22 |
| | No: Claims | |
| Industrial applicability (IA) | Yes: Claims | 1-17,19-22 |
| | No: Claims | 18 |

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

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Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 18 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

- D1: WO 02/00679 A (NOVARTIS ERFIND VERWALT GMBH ; NOVARTIS AG (CH); BEATTIE DAVID (GB); C) 3 January 2002 (2002-01-03)
- D2: GB-A-1 514 476 (GLAXO LAB LTD) 14 June 1978 (1978-06-14)
- D3: US-A-3 856 828 (PHILLIPPS G ET AL) 24 December 1974 (1974-12-24)
- D4: UENO H ET AL: "Synthesis and evaluation of antiinflammatory activities of a series of corticosteroid 17.alpha.-esters containing a functional group" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 34, no. 8, 1 August 1991 (1991-08-01), pages 2468-2473, XP002086576 ISSN: 0022-2623
- D5: WO 89/03390 A (BODOR NICHOLAS S) 20 April 1989 (1989-04-20)
- D6: GB-A-2 079 755 (OTSUKA PHARMA CO LTD) 27 January 1982 (1982-01-27)
- D7: GB-A-2 137 206 (GLAXO GROUP LTD) 3 October 1984 (1984-10-03)
- D8: GB-A-1 384 372 (GLAXO LAB LTD) 19 February 1975 (1975-02-19)

2. Novelty

The claimed subject matter is concerned with androstene steroid compounds. None of the documents of the search report disclose such compound.

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The distinguishing feature of the molecule is the cyano group, indeed the documents D1-D8 disclose steroid of similar structure with the difference that instead of the cyano moiety they have alkyl (eg. Me), halogen, ester....

The claimed subject matter can be considered as novel.

3. Inventive step

Document D1, could be considered to represent the most relevant state of the art, discloses (cf. examples 14,24 and claim 1) a steroid from which the subject-matter of claim 1 differs (at least one feature) in that cyano-ester on position 17 of ring system instead of methyl-ester. Beside this, other structural features are different (in total 3 different technical feature).

The problem to be solved by the present invention may therefore be regarded as to provide a novel steroid useful as anti-inflammatory.

None of the documents cited in the search report neither alone or combined together would have led the skilled person to this specific steroid as claimed and foresee that such compound would still exert anti-inflammatory activities.

The claimed subject matter can be considered as inventive.

Re Item VII

Certain defects in the international application

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D8 is not mentioned in the description, nor are these documents identified therein.

Even though these documents are cited as A category in the search report, they should be mentioned in the description because no other prior art have been cited.

Re Item VIII

Certain observations on the international application

1)For the assessment of the present claim 8 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for

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example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

- 2) In claim 1, the term "substituted" aryl or heteroaryl defining R1 should be clarified or removed.